DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

95089d

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

NOV 16 2004

WARNING LETTER

FEDERAL EXPRESS

Dr. Ingeborg Hochmair
CEO
MED-EL ELEKTRO-MEDIZINISCHE GERÄTE GmbH
Furstenweg 77a, A-6020
Innsbruck, Austria

Dear Dr. Hochmair:

During inspections of your firms, MED-EL ELEKTRO-MEDIZINISCHE GERÄTE GmbH, located in Innsbruck, Austria on June 7 through June 16, 2004, our investigators determined that your firms manufacture cochlear implant systems. Cochlear implants, such as the COMBI C40+,the PULSAR,are devices within the meaning of section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act)(21 U.S.C. § 321(h)).

These inspections revealed that your devices appear to be adulterated within the meaning of section 501(h) of the Act (21 U.S.C. § 351(h)), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820. Significant violations include, but are not limited to, the following:

1. Failure to establish and maintain procedures to control the design of the device in order to ensure that specified design requirements are met, as required by 21 CFR 820.30 (a)(1). For example, procedures to control the design process for the device were not implemented [redacted] was not implemented. The requirements for design control were not used and design control procedures were not followed for the product change ([redacted] from a thick film to thin film product. There was also a change in components (materials) which resulted in changes to the finished product.

2. Failure to establish and maintain procedures for the identification, documentation, validation or where appropriate verification, review, and approval of design changes before their implementation, as required by 21 CFR 830.30(i). For example, the firm failed to implement Quality System regulation design control requirements for changing the ceramic housing assembly components ([redacted]. Your firm failed to provide documentation for design and development planning, design input, design output, design review, design verification, design transfer, and design history file for changing the [redacted]s. Your firm's Standard Operating Procedure for Design Control ([redacted], page 9, does not provide enough detail to meet the requirements in 21 CFR 820.30(i).

3. Failure to maintain procedures to ensure that the design requirements relating to a device are appropriate and address the intended use of the device including the needs of the user and patient. The procedure shall include a mechanism for addressing incomplete, ambiguous, or conflicting requirements. The design input requirements shall be documented and shall be reviewed and approved by a designated individual(s), as required by 21 CFR 820.30(c). For example, the SOP, "[redacted] including [redacted] and [redacted]" was not followed. The [redacted] process was used to change the C40+ housing assembly from a "thick" to "thin" film. There were no design input requirements for changing the product characteristics/specifications-material, and material thickness changes to the [redacted]. There were no design input requirements/specifications for [redacted] specifications and [redacted] (e.g. [redacted], [redacted] test, [redacted], [redacted] and [redacted] test).

4. Failure to establish and maintain procedures for validating the device design, as required by 21 CFR 820.30(g). For example, Design Verification/Validation [redacted] was

not followed. There was no verification or validation (V&V) plan. Review and approval of the V&V plan before various verification activities were not conducted on the "[redacted]" products. Your firm did not place in-coming requirements on the [redacted], i.e. thickness or chemical uniformity and distribution from [redacted]

5. Failure to establish and maintain a DHF for each type of device. The DHF shall contain or reference the records necessary to demonstrate that the design was developed in accordance with the approved design plan and the requirements, as required by 21 CFR 820.30(j). For example, design control procedure [redacted] was not implemented. Your firm failed to have a design history file for the change of materials in the [redacted] housing assembly and changes from using a thick film to a thin film process.

6. Failure to establish and maintain procedures for defining and documenting design output in terms that allow an adequate evaluation of conformance to design input requirements. Design output procedures shall contain or make reference to acceptance criteria and shall ensure that those design outputs that are essential for the proper functioning of the device are identified, as required by 21 CFR 820.30(d). For example, your firm failed to have design input requirements other than a [redacted] test from which acceptance criteria for design output could be identified. To control the manufacturing of a product, your firm must have detailed product and/or process specifications. Any product manufactured under controlled conditions must have detailed product specifications or detailed manufacturing process specifications. MED-EL fails to have product specifications or manufacturing process specifications for the [redacted] of the [redacted]

7. Failure to establish and maintain procedures to ensure that the device design is correctly translated into production specifications, as

required by 21 CFR 820.30(h). For example: (a) the new design using the [redacted] for the thin film technology was not validated before being implemented; (b) [redacted] has not been completed; (c) the thin film C40+ housing assembly and the [redacted] and/or the process for the [redacted] has not been characterized; and (d) design input requirements were not predetermined for transfer into production.

8. Failure to establish and maintain data that clearly describe or reference the specified requirements, including quality requirements, for purchased or otherwise received product and services, as required by 21 CFR 820.50(b). For example, MED-EL's [redacted] to [redacted] for purchase of the [redacted] housing assembly manufactured with a [redacted] lacks specific specifications regarding the [redacted] and/or specification for the [redacted] used to apply the [redacted]

9. Failure to establish and maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements. Each manufacturer shall establish and maintain the requirements, including quality requirements that must be met by suppliers, contractors, and consultants. Each manufacturer shall evaluate and select potential suppliers, contractors, and consultants on the basis of their ability to meet specified requirements, including quality requirements. The evaluation shall be documented, as required by 21 CFR 820.50(a)(1). For example, review of the "[redacted]" (supplier name was blank), dated August 17, 2001, failed to reference any [redacted] requirement for the supplier to meet the Quality System regulation. Changes to quality elements were mentioned, but requirements to meet the Quality System regulation were not mentioned. Product and manufacturing methods were discussed on the acceptance of returned products, which failed to comply with the Purchase Order or other written agreements specifications. However, your firm

failed to provide specifications or manufacturing methods identified for the [redacted] or method for applying the [redacted]. Although your firm performs supplier audits, there are no product and/or process operating specifications for the [redacted] Your firm failed to provide specific requirements that the supplier must meet in joining the [redacted] to the [redacted]

10. Failure to adequately maintain procedures to ensure that all purchased or otherwise received product and services conform to specified requirements, as required by 21 CFR 820.50. For example, review of SOP, "[redacted] dated [redacted], showed the [redacted] or designee, is responsible for completing the [redacted] Agreement. This procedure lacked specific instructions for [redacted] for a [redacted] to have a [redacted] requirement for a [redacted] to comply with the Quality System regulation.

11. Failure to define the type and extent of control to be exercised over the product, services, suppliers, contractors, and consultants, based on the evaluation results, as required by 21 CFR 820.50(a)(2). For example, [redacted] dated [redacted], showed that the [redacted] lacked process-operating and [redacted] which are required to produce and control the quality of the [redacted]

12. Failure to establish and maintain procedures for acceptance of incoming product. Incoming product shall be inspected, tested, or otherwise verified as conforming to specified requirements. Acceptance or rejection shall be documented, as required by 21 CFR 820.80(b). For example, procedures for acceptance or rejection of incoming products were not complete. Your firm failed to sample and conduct routine testing of the [redacted] between the [redacted] and [redacted]. These tests may include [redacted] test such as [redacted], [redacted] and others tests.

13. Failure to establish and maintain procedures for analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems. Appropriate statistical methodology shall be employed where necessary to detect recurring quality problems, as required by 21 CFR 820.100(a)(1). For example, there is no procedure addressing the data entry requirements for transferring information from complaint files to the electronic complaint database. The database is used for data analysis. All essential information from complaints and failure analysis information contained within each complaint was not transferred to the electronic complaint database.

14. Failure to establish and maintain procedures for investigating the cause of nonconformities relating to product, processes, and the quality system, as required by 21 CFR 820.100(a)(2). For example:

(a) a "loss of hermeticity," can cause failure of the [redacted] that could result in [redacted] Your firm failed to test explanted devices for DC leakage that were confirmed to have "Loss of Hermeticity" and the [redacted] out of specification. DC leakage was determined to be a critical specification in your firm's risk analysis for cochlear implants.

(b) Review of [redacted] showed that the facts did not support the conclusion that device failure could be related to an accident from trauma to the forehead area. There was no failure analysis information showing any failure attributable to stress on the device. The device failure analysis showed failure was due to "Loss of Hermeticity." There was no indication that the root cause of the hermeticity problem was different than the already established thick film process [redacted] reliability problems.

15. Failure to adequately maintain procedures for implementing corrective and preventive action, and failure to document all activities and results under this section, as required by 21 CFR 820.100(b). For example, [redacted] were reported to have been identified using a Scanning Electron Microscope(SEM) for element analysis. The test method and test [redacted] were not documented for the [redacted] analysis. Review of complaint and failure analysis records found photos without explanations. These photos were reported to document a variety of nonconformances including "Loss of Hermeticity" and nonconformance sites on the [redacted] The procedures lack a requirement for disclosing the reason for the photos and any nonconformance exhibited in the photos to support a device failure with evidence of "Loss of Hermeticity". The conclusion given as "The results of the examinations showed that the device was no longer working electrically within specifications," does not include all information that was reasonably known to the manufacturer.

16. Failure to establish and maintain procedures to control product that does not conform to specified requirements. The procedures shall address the identification, documentation, evaluation, segregation, and disposition of nonconforming product. The evaluation of nonconformance shall include a determination of the need for an investigation and notification of the persons or organizations responsible for the nonconformance. The evaluation and any investigation shall be documented, as required by 21 CFR 820.90(a). For example, failure analysis photos show surface contamination of electronic substrates. Even though some contamination was identified as dendrites, other contaminants had not been analyzed. All contaminants could potentially form DC leakage paths. The failure of the cochlear implant can result in pain, uncomfortably loud sound sensation, noise perceptions, etc., but the relationship of these patient perceptions to potential product failure modes is not explained in the failure investigations.

17. Failure to establish and maintain procedures that define the responsibility for review and the authority for the disposition of nonconforming product. The procedures shall set forth the review and disposition process. Disposition of nonconforming product shall be documented. Documentation shall include the justification for use of nonconforming product and the signature of the individual(s) authorizing the use, as required by 21 CFR 820.90(b)(1). For example, review of your firm's quarantined products found that cochlear implants returned from the US and documented as scrapped were, in fact, not scrapped.

18. Failure to maintain device master records (DMR`s) and to ensure that each DMR is prepared and approved in accordance with 21 CFR 820.40. The DMR for each type of device shall include, or refer to the location of, the following information: device specifications including appropriate drawings, composition, formulation, component specifications, and software specifications, as required by 21 CFR 820.181(a). For example, your firm failed to provide specifications for the [redacted] thickness and other [redacted] characteristics for the [redacted] such as bonding strength, peel, crush, leaching, tensile and shear.

19. Failure to establish and maintain procedures for identifying valid statistical techniques required for establishing, controlling, and verifying the acceptability of process capability and product characteristics where appropriate, as required by 21 CFR 820.250(a). For example, there is no information to support the appropriateness of the statistical techniques used, e.g., the number of test samples used to determine acceptability of thick film C40+ [redacted] housing assembly for "equal or better," which is used as a reference for the verification testing of the thin film devices.

In addition, we have included two violations from the Quality System regulation that were listed on the FDA 483 that was issued at the conclusion of the March 29 - April 1, 2004, inspection of MED-EL, as follows:

1. Failure to provide procedures addressing the data entry requirements for transferring information from complaint files to the electronic complaint database. The database is used for data analysis. When all essential information from complaints and failure analysis fails to provide the results of a process, which cannot be fully verified by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedures, as required by 21 CFR 820.75. For example, your firm failed to comply with the requirements of the government standard that is reported by used during validation of the ETO sterilization process. MED-EL stated during the inspection that ETO validation was conducted according to the British Standard EN550:1994 and performance qualification using B3.4.4 Method C: Half-cycle method (EIR - 3/29-4/1/04-pg.9 & 10). Review of the firm's validation test data indicated that the [redacted] half cycle runs were not performed at the worst case cycle parameter specification of [redacted] ETO gas (the minimum gas concentration specified). The [redacted] validation runs were performed with gas concentrations at [redacted] and [redacted]

   Your [redacted] response, [redacted] appears to be adequate.

2. Failure to adequately establish procedures for quality audits and conduct such audits to assure that the quality system is in compliance with the established quality system requirements and to determine the effectiveness of the quality system as required by 21 CFR 820.22. For example, a review of [redacted] and [redacted] procedure lacked specific procedures for conducting an audit of a contract sterilizer. [redacted] states that to facilitate the auditor's investigations, there may be checklists, recording forms and forms to document non-conformance.

Your firm's [redacted] response appears to be adequate. However, your firm should specify the affected personnel that will be trained on the procedure and checklist. The length of time between the annual audit and the second audit should be specified. Please provide the checklists, recording forms and forms that document nonconformance.

Additionally, the June 7 through June 16, 2004, inspection of MED-EL revealed that your devices are misbranded within the meaning of section 502(t)(2)of the Act, in that your firm failed or refused to furnish any material of information required by or under section 519 respecting the device and 21 CFR Part 803 - Medical Device Reporting (MDR) regulation. Significant deviations include, but are not limited to the following:

1. Failure to provide documentation and recordkeeping information that facilitates timely follow-up and inspection by FDA, as required by 21 CFR 803.17(b)(1).

   (a) For example, [redacted] does not have sufficient requirements to verify that an MDR forwarded to MED-EL Corporation (North America) for transmission to the FDA was sent to the FDA.

   (b) Manufacturer report [redacted] was reportedly filed with FDA. A search of the FDA MDR database showed no record of the filing and MED-EL Corp. (North Americas) could not provide evidence that the report had been transmitted (faxed) to FDA.

3. Failure to provide all MDR information to FDA, as required by 21 CFR 803.50. For example, review of MDRs for cochlear explants resulting from a loss of hermeticity reported the failure mode as electronically no longer working within specifications. The manufacturer was aware that the root cause of these failures was a "Loss of Hermeticity." There were over [redacted] MDR reports

attributing device failure to "out of specification" devices, without reporting the root cause of the failure as due to a "Loss of Hermeticity." Additionally, your firm was aware that many of the "loss of hermeticity" devices showed evidence of [redacted] and [redacted] on the [redacted], which accounts for some of the pain experienced by device users.

This letter is not intended to be an all-inclusive list of violations at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, Form FDA 483 (FDA 483), issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to correct the violations and to bring your products into compliance.

Given the serious nature of these violations of the Act, cochlear implants (COMBI 40+, C40+ S(compressed), and C40+ (GB))manufactured by your firm, imported or offered for import are subject to refusal of admission under section 801(a) of the Act, 21 U.S.C. § 381(a), in that they appear to be adulterated. As a result, FDA may take steps to refuse these products, known as "detained without physical examination," until these violations are corrected.

In order to remove the devices from detention, you should provide a written response to this Warning Letter as described below and correct the violations described in this letter. We will notify you if your response is adequate, and we may need to re-inspect your facility to verify that the appropriate corrections have been made. In addition, U.S. federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of government contracts.

A response from you, dated [redacted], concerning our investigators' observations noted on the FDA 483 was sent

to us. However, we did not receive your response until [redacted] and are currently reviewing all of the documents. We will continue our review of these documents and communicate our comments to you in a separate letter. In the meantime, however, you should not delay your response to this warning letter.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter, of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include all documentation of the corrective action you have taken. If you plan to make any corrections in the future, include those plans with your response to this letter as well. If the documentation is not in English, please provide a translation to facilitate our review.

Your response should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement A, Dental, ENT, and Ophthalmic Devices Branch, 2098 Gaither Road, Rockville, Maryland 20850 USA, to the attention of Ronald L. Swann.

If you need help in understanding the contents of this letter, please contact Betty W. Collins, Director, Division of Enforcement A at (301) 594-4611.

For technical questions, please contact Valerie A. Flournoy at the above address or at (301) 594-4613 or FAX (301) 594-4638.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health